Focus on Meiosis

Mary Herbert

Newcastle Fertility Centre, International Centre for Life, Times Square, Newcastle upon Tyne NE1 4EP, UK

Correspondence should be addressed to M Herbert; Email: mary.herbert@ncl.ac.uk

The past five years have seen the dawn of an era of illumination in our understanding of how vertebrate meiosis is regulated. Much of the foundation for recent progress came from the enormous advances in elucidating the molecular regulation of mitotic cell division and yeast meiosis (reviewed in Uhlmann 2001, Petronczki et al. 2003, Watanabe 2005). Translating these advances into an understanding of how mammalian meiosis is regulated provides promise in the treatment and prevention of disease from two different perspectives. Firstly, it will enable us to better understand the underlying causes of aneuploidies such as Down syndrome, which predominantly arise during maternal meiosis I (Lamb et al. 1996). Secondly, deciphering the mechanisms of cell cycle regulation in oocytes will provide a framework in which strategies for successful therapeutic cloning can be developed.

The articles included in this issue provide comprehensive updates taking us on the fascinating journey from meiotic recombination to fertilisation. In an extensive and thought-provoking review focussing on early events of meiosis, Meisha Morelli and Paula Cohen explore the different checkpoint responses of male and female germ cells. Drawing on evidence from a wide range of mouse meiotic mutants, they present a picture in which male prophase germ cells are less tolerant of recombination defects than their female counterparts. This is consistent with the majority of human aneuploidies being of maternal rather than paternal origin (Lamb et al. 1996). In the second review Ekaterina Revenkova and Rolf Jessberger, who discovered the meiosis-specific cohesin sub-unit SMC1B (Revenkova et al. 2004) address the issue of how sister chromatids are held together in mammalian meiosis. The emerging picture is that meiotic and mitotic cohesins co-exist during mammalian meiosis I, giving rise to three, possibly four, distinct cohesin complexes (Revenkova & Jessberger 2005). Elucidating the functional significance of these different complexes will no doubt provide fertile ground for future insights into the regulation of the two-step loss of cohesion – first from sister arms in meiosis I and then from sister centromeres in meiosis II.

The next three review articles in this issue focus exclusively on the oocyte. In mammals, the formation of a competent female gamete is a tortuous process that, in the case of humans can take decades to complete. Mammalian oocytes enter meiosis during fetal life when pairs of homologous chromosomes synapse, form crossovers during recombination, and remain physically connected at cytologically distinct structures known as chiasmata (reviewed by Morelli & Cohen 2005). Disjunction of homologues requires resolution of chiasmata, which does not normally occur until the oocyte resumes meiosis following exposure to the pre-ovulatory surge of luteinizing hormone (LH), after the animal has reached sexual maturity. Resumption of meiosis also occurs spontaneously when fully grown oocytes are removed from their follicular environments (Pincus & Enzmann 1935), indicating that intra-follicular inhibitory factors are responsible for maintaining prophase arrest. Recent findings from Laurinda Jaffe and Lisa Mehlmann indicate that prophase arrest is maintained through stimulation of the Gs G-protein by the G-protein coupled receptor GPR3 which induces elevated levels of cAMP in the oocyte (Mehlmann et al. 2004, Mehlmann 2005). Here Lisa Mehlmann provides an update on the current state of knowledge on the regulation of meiotic arrest and proposes mechanisms by which the pre-ovulatory LH surge induces resumption of meiosis.

Following resumption of meiosis, the oocyte initiates a rare feat of choreography in which the hazardous business of homologue segregation must be co-ordinated with the migration of the meiosis I spindle from the central to the cortical region of the oocyte. This is important because initiation of anaphase prior to arrival of the spindle at the cortex would result in an excessive loss of cytoplasm to the polar body, which would likely compromise the viability of any resulting embryo. The review by Stephan Brunet and Bernard Maro focuses on the bizarre process by which the meiosis I spindle is constructed in the absence of centrosomes, and largely in the absence of stable microtubule attachments. They also review the emerging molecular players involved in mediating spindle migration and asymmetric cell division. Keith Jones concludes the series of reviews by addressing the molecular regulation of progression through meiosis I, arrest at metaphase of meiosis II and egg activation with a special emphasis on the pivotal role of calcium signalling in these processes.
It was a great pleasure to be invited to guest edit this exciting issue and I would like to thank the authors for their excellent contributions.

References


